

Amendment Dated December 13, 2005

Reply to Office Action of September 30, 2005

Amendments to the Claims: This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims

1. (Canceled)

2. (Previously Presented) The process according to claim 49, wherein P is a tetrahydropyranyl (THP) protecting group.

3. (Previously Presented) The process according to claim 49 or claim 2, wherein X is iodine.

4. (Previously Presented) The process according to claim 49, wherein A is (CH₂)₂Ph, ---- represents a double bond, P is THP and X is I.

5.-7. (Canceled)

8. (Previously Presented) The process according to claim 55, wherein P is a tetrahydropyranyl (THP) protecting group.

9. (Previously Presented) The process according to claim 55, wherein A is (CH₂)₂Ph, ---- represents a double bond and P is THP.

10.-12. (Canceled)

13. (Previously Presented) The process according to claim 58, wherein P is a tetrahydropyranyl (THP) protecting group.

14. (Previously Presented) The process according to claim 58, wherein A is (CH₂)₂Ph, ---- represents a double bond and P is THP.

15.-17. (Canceled)

18. (Previously Presented) The process according to claim 61, wherein P is a tetrahydropyranyl (THP) protecting group.

19. (Previously Presented) The process according to claim 61 or claim 18, wherein A is $(CH_2)_2Ph$ and ---- represents a double bond.

20.-22. (Canceled)

23. (Previously Presented) The process according to claim 64, wherein P is a tetrahydropyranyl (THP) protecting group.

24. (Previously Presented) The process according to claim 64, wherein A is $(CH_2)_2Ph$, P is THP, ---- represents a double bond, and compound (VIIa) reacts to give compound (VIa).

25. (Previously Presented) The process according to claim 64, wherein A is $(CH_2)_2Ph$, P is THP, ---- represents a double bond, and compound (VIIb) reacts to give compound (VIb).

26. (Previously Presented) The process according to claim 64, wherein A is $(CH_2)_2Ph$, ---- represents a double bond, and compound (VIIc) reacts to give compound (VIc).

27.-29. (Canceled)

30. (Previously Presented) The process according to claim 67, wherein P is a tetrahydropyranyl (THP) protecting group.

31. (Previously Presented) The process according to claim 67, wherein A is $(CH_2)_2Ph$, P is THP and compound (VIa) reacts to give compound (Va).

32. (Previously Presented) The process according to claim 67, wherein A is $(CH_2)_2Ph$, P is THP and compound (VIb) reacts to give compound (Vb).

33. (Previously Presented) The process according to claim 67, wherein A is $(CH_2)_2Ph$ and compound (VIc) reacts to give compound (Vc).

34. (Canceled)

35. (Previously Presented) The process according to claim 70, wherein P is a tetrahydropyranyl (THP) protecting group.

36. (Previously Presented) The process according to claim 70, wherein A is $(CH_2)_2Ph$, P is THP, —— represents a single bond, and compound (Va) reacts to give compound (IVa).

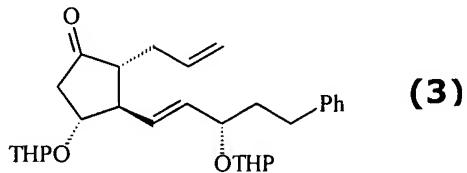
37. (Previously Presented) The process according to claim 70, wherein A is $(CH_2)_2Ph$, P is THP, —— represents a single bond, and compound (Vb) reacts to give compound (IVb).

38. (Previously Presented) The process according to claim 70, wherein A is $(CH_2)_2Ph$, —— represents a single bond, and compound (Vc) reacts to give compound (IVc).

39.-40. (Canceled)

41. (Original) A process for synthesising Latanoprost comprising the steps of:

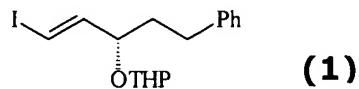
a) preparing a compound of formula (3):



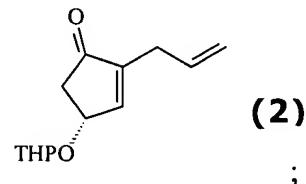
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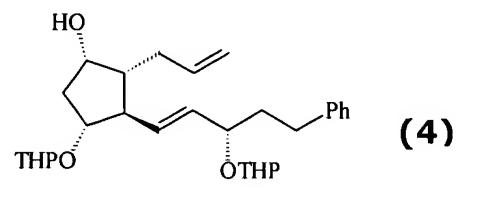
said preparing comprising converting a compound of formula (1):



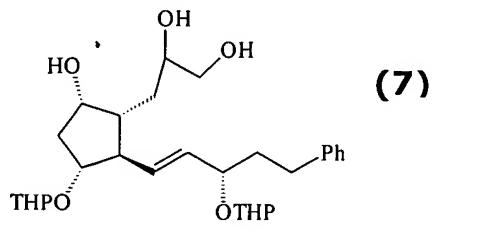
to a cuprate reagent and performing a 1,4 addition reaction between the cuprate reagent and a compound of formula (2):



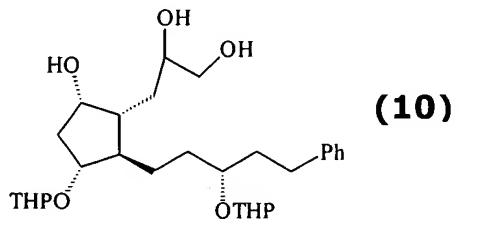
b) selectively reducing the compound of formula (3) to provide a compound of formula (4):



c) dihydroxylating the compound of formula (4) to provide a compound of formula (7):



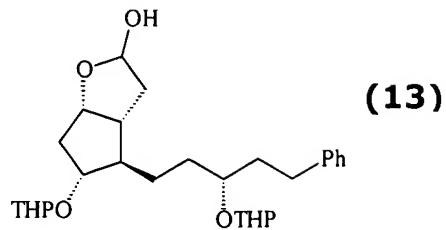
d) reducing the compound of formula (7) to provide a compound of formula (10):



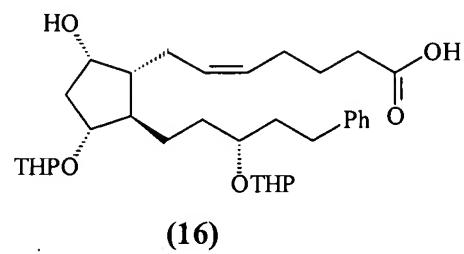
e) performing a diol cleavage reaction on the compound of formula (10) to provide a compound formula (13):

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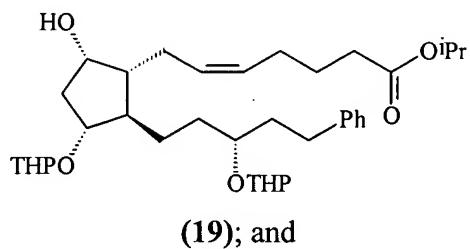
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- f) performing a Wittig reaction on the compound of formula (13) to provide a compound of formula (16):



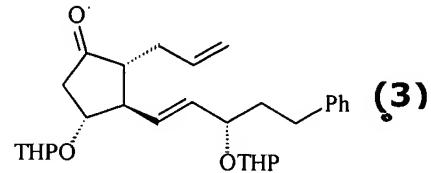
- g) esterifying the compound of formula (16) to provide a compound of formula (19):



- h) deprotecting the compound of formula (19) to provide Latanoprost.

42. (Previously Presented) A process for synthesising Latanoprost comprising the steps of:

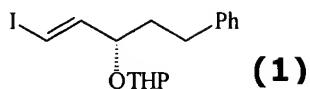
- a) preparing a compound of formula (3):



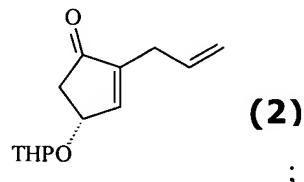
said preparing comprising converting a compound of formula (1):

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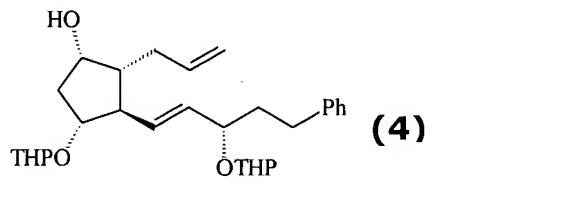
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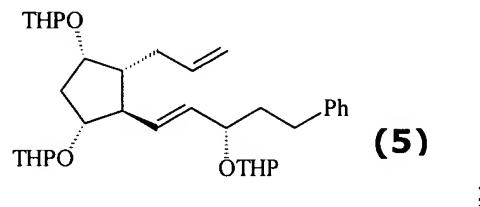
to a cuprate reagent and performing a 1,4 addition reaction between the cuprate reagent and a compound of formula (2):



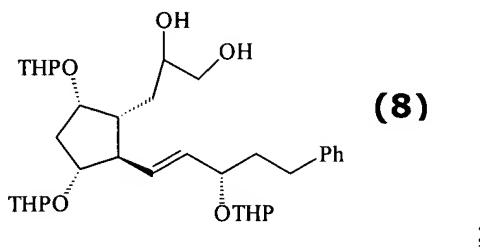
- b) selectively reducing the compound of formula (3) to provide a compound of formula (4):



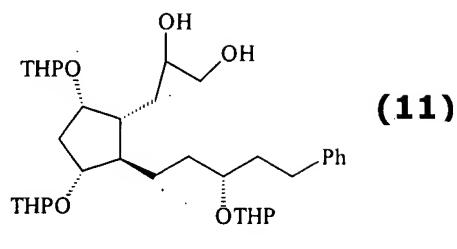
- c) protecting the compound of formula (4) to provide a compound of formula (5):



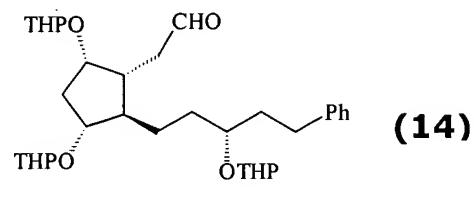
- d) dihydroxylating the compound of formula (5) to provide a compound of formula (8):



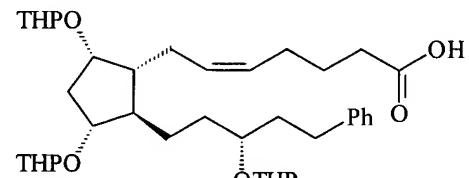
- e) reducing the compound of formula (8) to provide a compound of formula (11):



- f) performing a diol cleavage reaction on the compound of formula (11) to provide a compound of formula (14):

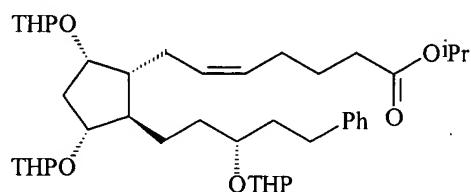


- g) performing a Wittig reaction on the compound of formula (14) to provide a compound of formula (17):



(17);

- h) esterifying the compound of formula (17) to provide a compound of formula (20):



(20); and

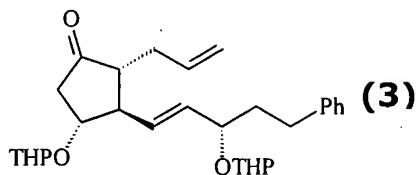
- i) deprotecting the compound of formula (20) to provide Latanoprost.

43. (Original) A process for synthesising Latanoprost comprising the steps of:

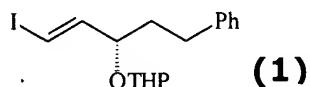
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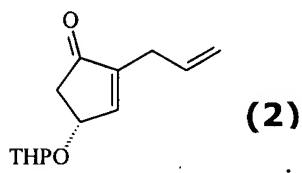
- a) preparing a compound of formula (3):



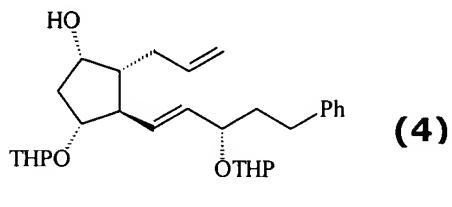
said preparing comprising converting a compound of formula (1):



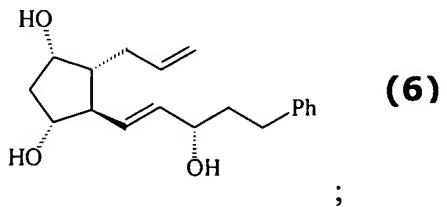
to a cuprate reagent and performing a 1,4 addition reaction between the cuprate reagent and a compound of formula (2):



- b) selectively reducing the compound of formula (3) to provide a compound of formula (4):



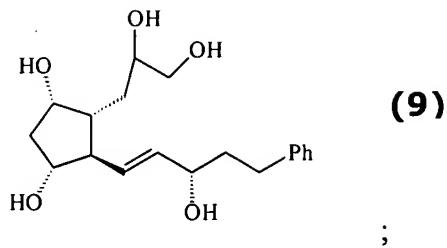
- c) deprotecting the compound of formula (4) to provide a compound of formula (6):



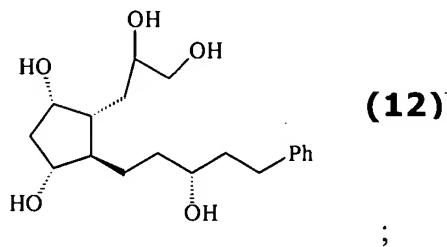
- d) dihydroxylating the compound of formula (6) to provide a compound of formula (9):

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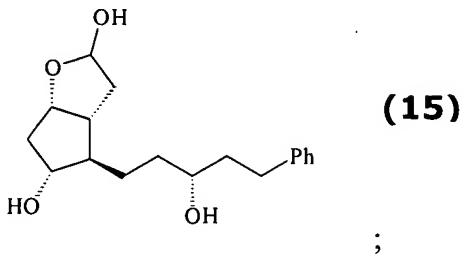
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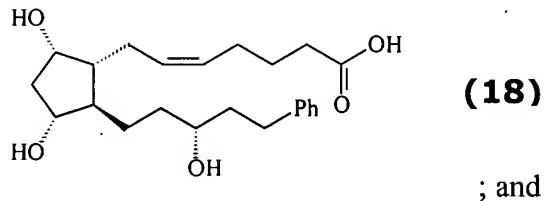
- e) reducing the compound of formula (9) to provide a compound of formula (12):



- f) performing a diol cleavage reaction on the compound of formula (12) to provide a compound of formula (15):



- g) performing a Wittig reaction on the compound of formula (15) to provide a compound of formula (18):



; and

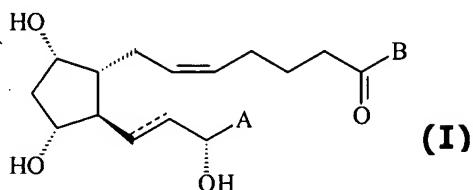
- h) esterifying the compound of formula (18) to provide Latanoprost.

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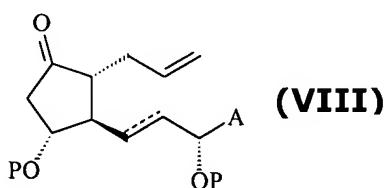
44.-48. (Canceled)

49. (Previously Presented) A process for the preparation of a prostaglandin compound having the formula (I):



wherein A is selected from the group consisting of C₁-C₆ alkyl groups; C₇-C₁₆ aralkyl groups wherein an aryl portion thereof is unsubstituted or substituted with one to three substituents selected from the group consisting of C₁-C₆ alkyl groups, halo and CF₃; and (CH₂)_nOR' wherein n is an integer from 1 to 3 and R' represents a C₆-C₁₀ aryl group which is unsubstituted or substituted with one to three substituents selected from the group consisting of C₁-C₆ alkyl groups, halo and CF₃; B is selected from OR'' and NHR'' wherein R'' is C₁-C₆ alkyl groups; and ---- represents a double bond or a single bond;

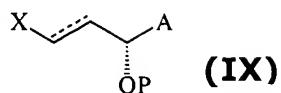
the process comprising a step of preparing a compound of formula (VIII):



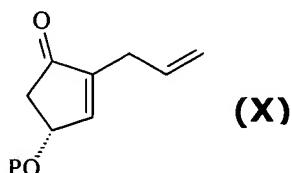
wherein A is selected from the group consisting of C₁-C₆ alkyl groups; C₇-C₁₆ aralkyl groups wherein an aryl portion thereof is unsubstituted or substituted with one to three substituents selected from the group consisting of C₁-C₆ alkyl groups, halo and CF₃; and (CH₂)_nOR' wherein n is an integer from 1 to 3 and R' represents a C₆-C₁₀ aryl group which is unsubstituted or substituted with one to three substituents selected from the group consisting of C₁-C₆ alkyl groups, halo and CF₃; P is a hydroxyl protecting group; and ---- represents a double bond or a single bond; said step comprising converting a compound of formula (IX):

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wherein A, P and --- are as defined above and X is a leaving group, to a cuprate reagent and performing a 1,4 addition reaction between the cuprate reagent and a compound of formula (X):

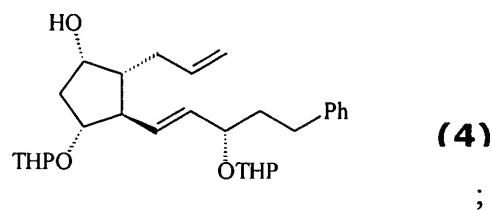


wherein P is as defined above.

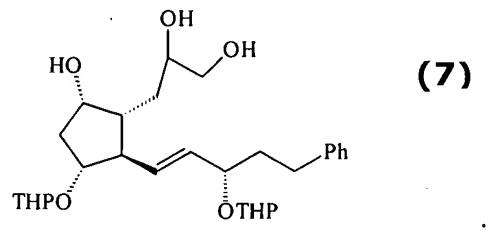
50. (Previously Presented) The process according to claim 2, wherein the compound having the formula (I) is Travoprost.

51. (Previously Presented) The process according to claim 49, wherein the compound having the formula (I) is Travoprost.

52. (Previously Presented) The process according to claim 49, wherein A is $\text{CH}_2\text{CH}_2\text{-Ph}$, --- represents a double bond and P is THP, the process further comprising selectively reducing the compound of formula (VIII) to provide a compound of formula (4):



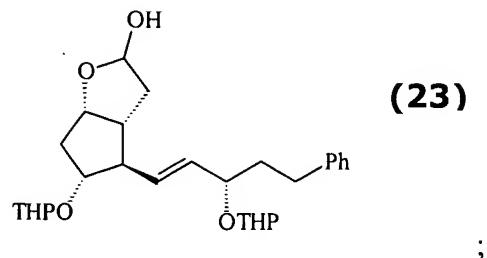
dihydroxylating the compound of formula (4) to provide a compound of formula (7):



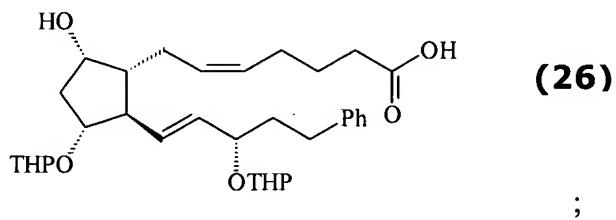
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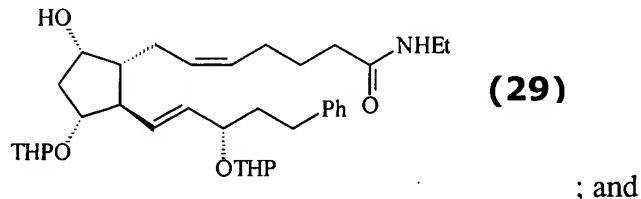
performing a diol cleavage reaction on the compound of formula (7) to provide a compound of formula (23):



performing a Wittig reaction on the compound of formula (23) to provide a compound of formula (26):

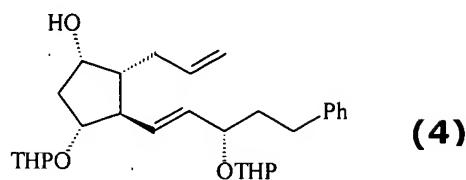


amidating the compound of formula (26) to provide a compound of formula (29):

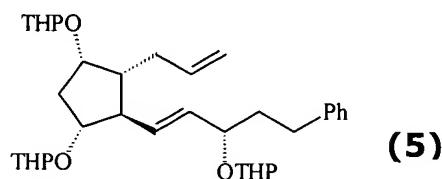


deprotecting the compound of formula (29) to provide Bimatoprost.

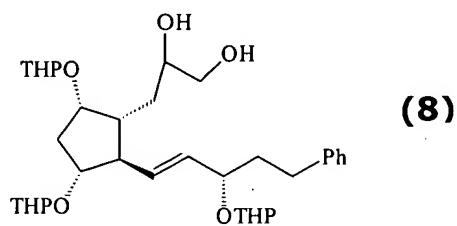
53. (Previously Presented) The process according to claim 49, wherein A is CH₂CH₂-Ph, —— represents a double bond and P is THP, the process further comprising selectively reducing the compound of formula (VIII) to provide a compound of formula (4):



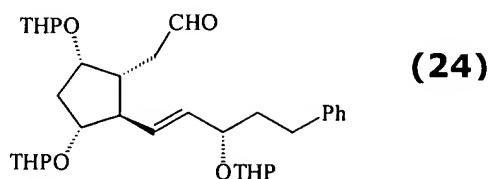
protecting the compound of formula (4) to provide a compound of formula (5):



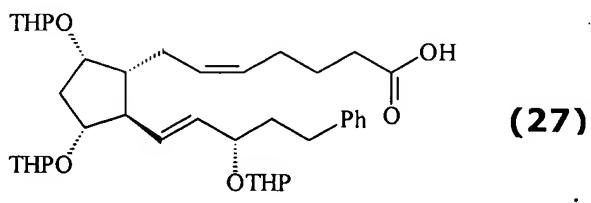
dihydroxylating the compound of formula (5) to provide a compound of formula (8):



performing a diol cleavage reaction on the compound of formula (8) to provide a compound of formula (24):



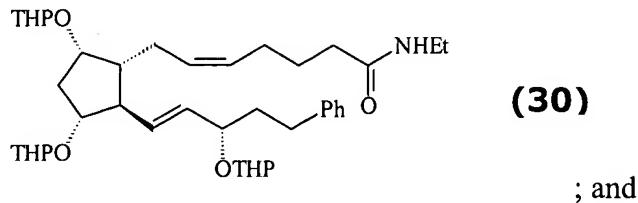
performing a Wittig reaction on the compound of formula (24) to provide a compound of formula (27):



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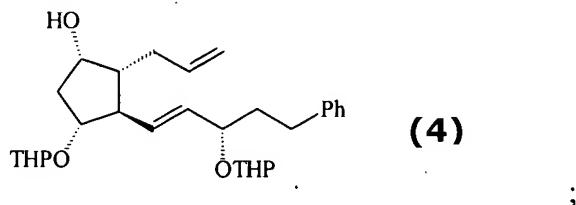
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amidating the compound of formula (27) to provide a compound of formula (30):

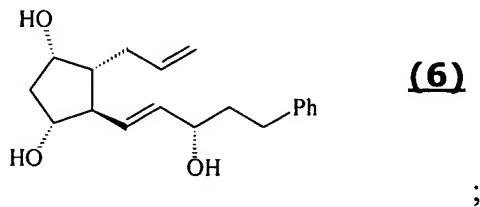


deprotecting the compound of formula (30) to provide Bimatoprost.

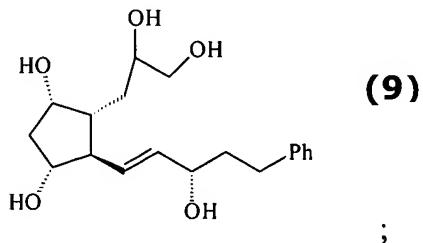
54. (Currently Amended) The process according to claim 49, wherein A is CH₂CH₂-Ph, —— represents a double bond and P is THP, the process further comprising selectively reducing the compound of formula (VIII) to provide a compound of formula (4):



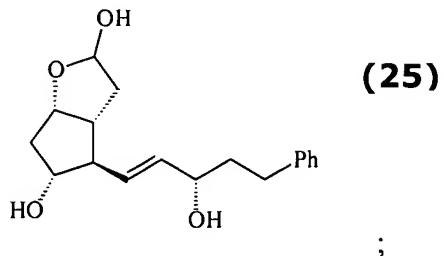
deprotecting the compound of formula (4) to provide a compound of formula (6):



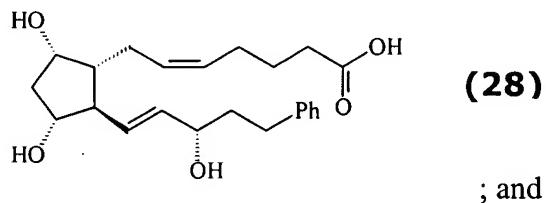
dihydroxylating the compound of formula (6) to provide a compound of formula (9):



performing a diol cleavage on the compound of formula (9) to provide a compound of formula (25):

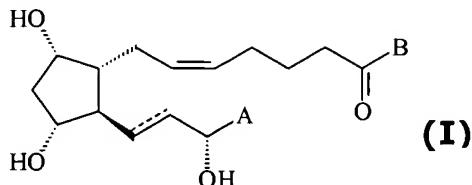


performing a Wittig reaction on the compound of formula (25) to provide a compound of formula (28):



amidating the compound of formula (28) to provide Bimatoprost.

55. (Previously Presented) A process for the preparation of a prostaglandin compound having the formula (I):



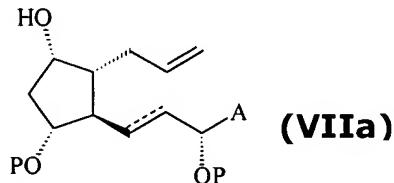
wherein A is selected from the group consisting of C₁-C₆ alkyl groups; C₇-C₁₆ aralkyl groups wherein an aryl portion thereof is unsubstituted or substituted with one to three substituents selected from the group consisting of C₁-C₆ alkyl groups, halo and CF₃; and (CH₂)_nOR' wherein n is an integer from 1 to 3 and R' represents a C₆-C₁₀ aryl group which is unsubstituted or substituted with one to three substituents selected from the group consisting of C₁-C₆ alkyl groups, halo and CF₃; B is

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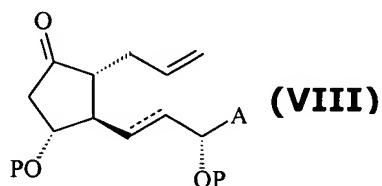
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selected from OR" and NHR" wherein R" is C₁-C₆ alkyl groups; and —— represents a double bond or a single bond;

the process comprising a step of preparing a compound of formula (VIIa):



wherein A is selected from the group consisting of C₁-C₆ alkyl groups; C₇-C₁₆ aralkyl groups wherein an aryl portion thereof is unsubstituted or substituted with one to three substituents selected from the group consisting of C₁-C₆ alkyl groups, halo and CF₃; and (CH₂)_nOR' wherein n is an integer from 1 to 3 and R' represents a C₆-C₁₀ aryl group which is unsubstituted or substituted with one to three substituents selected from the group consisting of C₁-C₆ alkyl groups, halo and CF₃; P is a hydroxyl protecting group and —— represents a double bond or a single bond;
said step comprising selectively reducing a compound of formula (VIII):



wherein A, P and —— are as defined above.

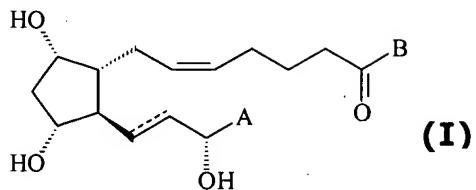
56. (Previously Presented) The process according to claim 8, wherein the compound having the formula (I) is Travoprost.

57. (Previously Presented) The process according to claim 55, wherein the compound having the formula (I) is Travoprost.

58. (Previously Presented) A process for the preparation of a prostaglandin compound having the formula (I):

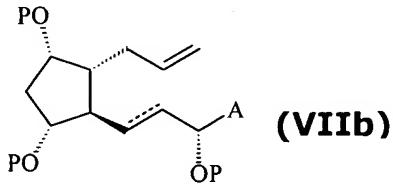
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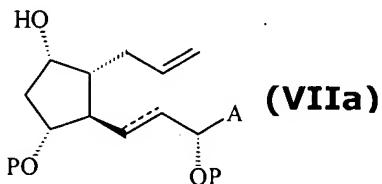


wherein A is selected from the group consisting of C₁-C₆ alkyl groups; C₇-C₁₆ aralkyl groups wherein an aryl portion thereof is unsubstituted or substituted with one to three substituents selected from the group consisting of C₁-C₆ alkyl groups, halo and CF₃; and (CH₂)_nOR' wherein n is an integer from 1 to 3 and R' represents a C₆-C₁₀ aryl group which is unsubstituted or substituted with one to three substituents selected from the group consisting of C₁-C₆ alkyl groups, halo and CF₃; B is selected from OR'' and NHR'' wherein R'' is C₁-C₆ alkyl groups; and --- represents a double bond or a single bond;

the process comprising a step of preparing a compound of formula (VIIb):



wherein A is selected from the group consisting of C₁-C₆ alkyl groups; C₇-C₁₆ aralkyl groups wherein an aryl portion thereof is unsubstituted or substituted with one to three substituents selected from the group consisting of C₁-C₆ alkyl groups, halo and CF₃; and (CH₂)_nOR' wherein n is an integer from 1 to 3 and R' represents a C₆-C₁₀ aryl group which is unsubstituted or substituted with one to three substituents selected from the group consisting of C₁-C₆ alkyl groups, halo and CF₃; P is a hydroxyl protecting group and --- represents a double bond or a single bond;
said step comprising protecting a compound of formula (VIIa):

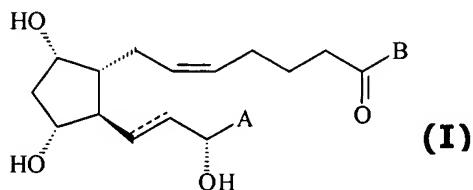


wherein A, P and --- are as defined above, with a hydroxyl protecting group.

59. (Previously Presented) The process according to claim 13, wherein the compound having the formula (I) is Travoprost.

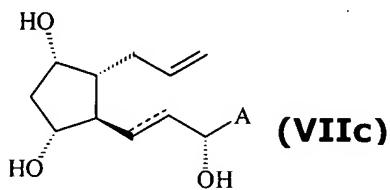
60. (Previously Presented) The process according to claim 58, wherein the compound having the formula (I) is Travoprost.

61. (Previously Presented) A process for the preparation of a prostaglandin compound having the formula (I):



wherein A is selected from the group consisting of C₁-C₆ alkyl groups; C₇-C₁₆ aralkyl groups wherein an aryl portion thereof is unsubstituted or substituted with one to three substituents selected from the group consisting of C₁-C₆ alkyl groups, halo and CF₃; and (CH₂)_nOR' wherein n is an integer from 1 to 3 and R' represents a C₆-C₁₀ aryl group which is unsubstituted or substituted with one to three substituents selected from the group consisting of C₁-C₆ alkyl groups, halo and CF₃; B is selected from OR'' and NHR'' wherein R'' is C₁-C₆ alkyl groups; and —— represents a double bond or a single bond;

the process comprising a step of preparing a compound of formula (VIIc):



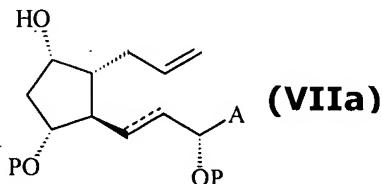
wherein A is selected from the group consisting of C₁-C₆ alkyl groups; C₇-C₁₆ aralkyl groups wherein an aryl portion thereof is unsubstituted or substituted with one to three substituents selected from the group consisting of C₁-C₆ alkyl groups, halo and CF₃; and (CH₂)_nOR' wherein n is an integer from 1 to 3 and R' represents a C₆-C₁₀ aryl group which is unsubstituted or substituted with

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one to three substituents selected from the group consisting of C₁-C₆ alkyl groups, halo and CF₃ and —— represents a double bond or a single bond;

said step comprising deprotecting a compound of formula (VIIa):

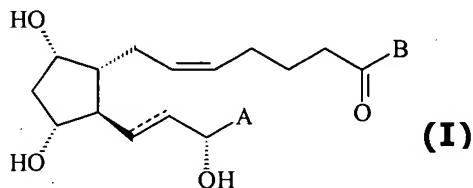


wherein A and —— are as defined above and P is a protecting group.

62. (Previously Presented) The process according to claim 18, wherein the compound having the formula (I) is Travoprost.

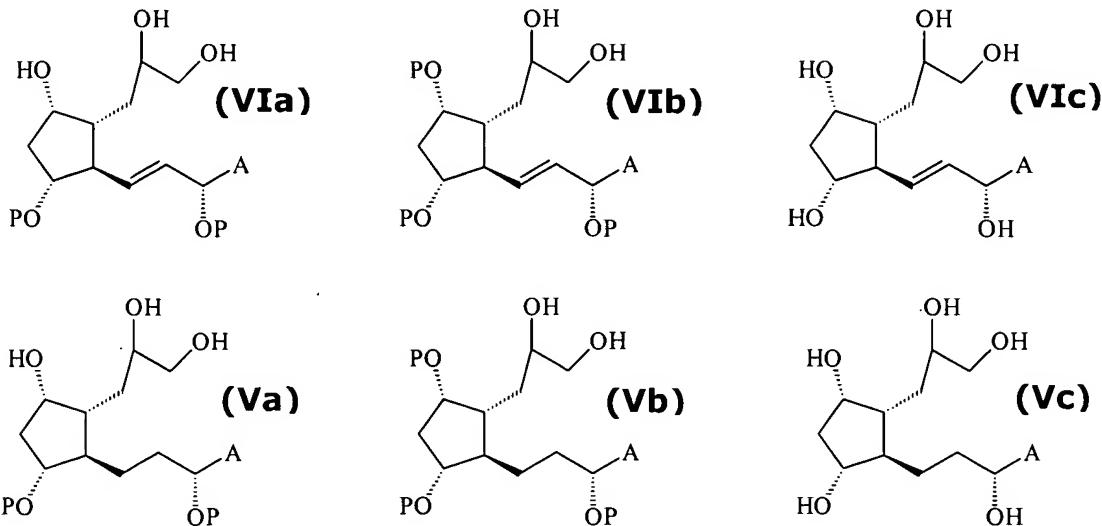
63. (Previously Presented) The process according to claim 61, wherein the compound having the formula (I) is Travoprost.

64. (Previously Presented) A process for the preparation of a prostaglandin compound having the formula (I):



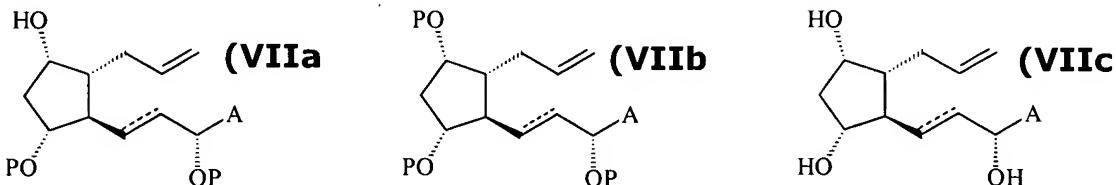
wherein A is selected from the group consisting of C₁-C₆ alkyl groups; C₇-C₁₆ aralkyl groups wherein an aryl portion thereof is unsubstituted or substituted with one to three substituents selected from the group consisting of C₁-C₆ alkyl groups, halo and CF₃; and (CH₂)_nOR' wherein n is an integer from 1 to 3 and R' represents a C₆-C₁₀ aryl group which is unsubstituted or substituted with one to three substituents selected from the group consisting of C₁-C₆ alkyl groups, halo and CF₃; B is selected from OR'' and NHR'' wherein R'' is C₁-C₆ alkyl groups; and —— represents a double bond or a single bond;

the process comprising a step of preparing a compound of formula (VIa), (VIb), (VIc), (Va), (Vb) or (Vc):



wherein A is selected from the group consisting of C₁-C₆ alkyl groups; C₇-C₁₆ aralkyl groups wherein an aryl portion thereof is unsubstituted or substituted with one to three substituents selected from the group consisting of C₁-C₆ alkyl groups, halo and CF₃; and (CH₂)_nOR' wherein n is an integer from 1 to 3 and R' represents a C₆-C₁₀ aryl group which is unsubstituted or substituted with one to three substituents selected from the group consisting of C₁-C₆ alkyl groups, halo and CF₃; and P is a hydroxyl protecting group;

said step comprising dihydroxylating a compound of formula (VIIa), a compound of formula (VIIb) or a compound of formula (VIIc):



wherein A and P are as defined above and —— is a double or single bond.

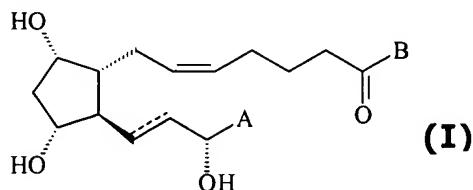
65. (Previously Presented) The process according to claim 23, wherein the compound having the formula (I) is Travoprost.

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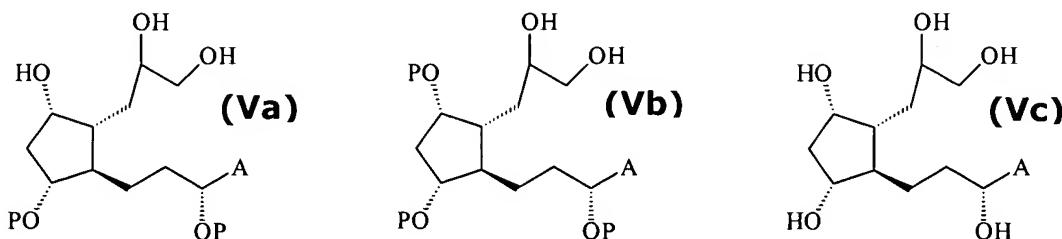
66. (Previously Presented) The process according to claim 64, wherein the compound having the formula (I) is Travoprost.

67. (Previously Presented) A process for the preparation of a prostaglandin compound having the formula (I):



wherein A is selected from the group consisting of C₁-C₆ alkyl groups; C₇-C₁₆ aralkyl groups wherein an aryl portion thereof is unsubstituted or substituted with one to three substituents selected from the group consisting of C₁-C₆ alkyl groups, halo and CF₃; and (CH₂)_nOR' wherein n is an integer from 1 to 3 and R' represents a C₆-C₁₀ aryl group which is unsubstituted or substituted with one to three substituents selected from the group consisting of C₁-C₆ alkyl groups, halo and CF₃; B is selected from OR'' and NHR'' wherein R'' is C₁-C₆ alkyl groups; and ---- represents a double bond or a single bond;

the process comprising a step of preparing a compound of formula (Va), (Vb) or (Vc):

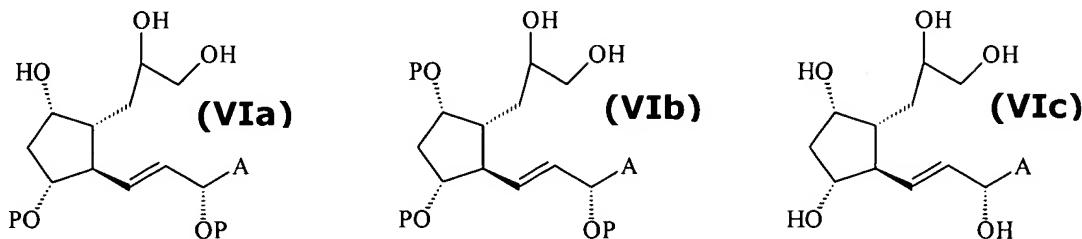


wherein A is selected from the group consisting of C₁-C₆ alkyl groups; C₇-C₁₆ aralkyl groups wherein an aryl portion thereof is unsubstituted or substituted with one to three substituents selected from the group consisting of C₁-C₆ alkyl groups, halo and CF₃; and (CH₂)_nOR' wherein n is an integer from 1 to 3 and R' represents a C₆-C₁₀ aryl group which is unsubstituted or substituted with one to three substituents selected from the group consisting of C₁-C₆ alkyl groups, halo and CF₃; and P is a hydroxyl protecting group;

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said step comprising reducing a double bond of a compound of formula (VIa), a compound of formula (VIb) or a compound of formula (VIc):

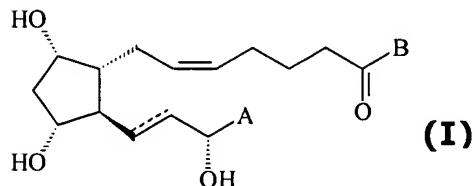


wherein A and P are as defined above.

68. (Previously Presented) The process according to claim 30, wherein the compound having the formula (I) is Travoprost.

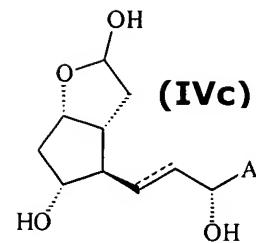
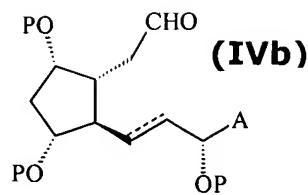
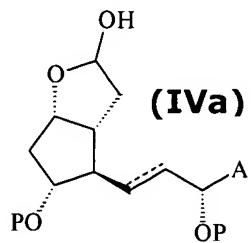
69. (Previously Presented) The process according to claim 67, wherein the compound having the formula (I) is Travoprost.

70. (Previously Presented) A process for the preparation of a prostaglandin compound having the formula (I):

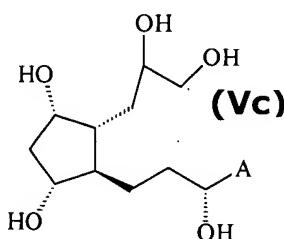
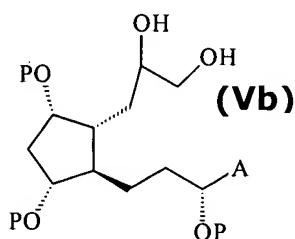
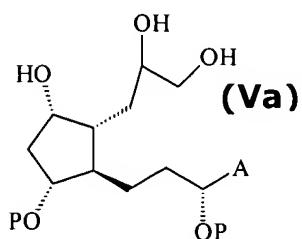
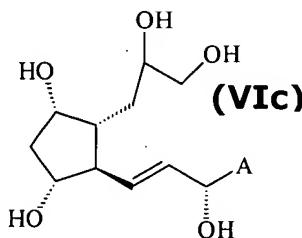
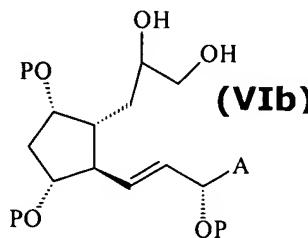
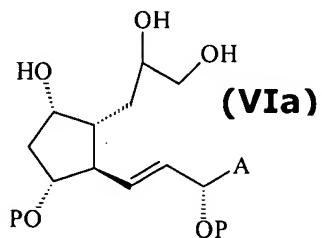


wherein A is selected from the group consisting of C₁-C₆ alkyl groups; C₇-C₁₆ aralkyl groups wherein an aryl portion thereof is unsubstituted or substituted with one to three substituents selected from the group consisting of C₁-C₆ alkyl groups, halo and CF₃; and (CH₂)_nOR' wherein n is an integer from 1 to 3 and R' represents a C₆-C₁₀ aryl group which is unsubstituted or substituted with one to three substituents selected from the group consisting of C₁-C₆ alkyl groups, halo and CF₃; B is selected from OR'' and NHR'' wherein R'' is C₁-C₆ alkyl groups; and —— represents a double bond or a single bond;

the process comprising a step of preparing a compound of formula (IVa), (IVb) or (IVc):



wherein A is selected from the group consisting of C₁-C₆ alkyl groups; C₇-C₁₆ aralkyl groups wherein an aryl portion thereof is unsubstituted or substituted with one to three substituents selected from the group consisting of C₁-C₆ alkyl groups, halo and CF₃; and (CH₂)_nOR' wherein n is an integer from 1 to 3 and R' represents a C₆-C₁₀ aryl group which is unsubstituted or substituted with one to three substituents selected from the group consisting of C₁-C₆ alkyl groups, halo and CF₃; P is a hydroxyl protecting group and —— represents a double bond or a single bond; said step comprising performing a diol cleavage reaction on a compound of formula (VIa), (Va), (VIb), (Vb), (VIc) or (Vc):



wherein A and P are as defined above.

71. (Previously Presented) The process according to claim 35, wherein the compound having the formula (I) is Travoprost.

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72. (Previously Presented) The process according to claim 70, wherein the compound having the formula (I) is Travoprost.